Complete Summary

GUIDELINE TITLE

Guidelines for the management of cutaneous warts.

BIBLIOGRAPHIC SOURCE(S)

Sterling JC, Handfield-Jones S, Hudson PM. Guidelines for the management of cutaneous warts. Br J Dermatol 2001 Jan; 144(1): 4-11. [51 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISCLAIMER

METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
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BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
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CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Cutaneous warts, including common warts, plane warts, intermediate warts, myrmecia, plantar warts, mosaic warts, anogenital warts, condyloma acuminata or venereal warts, and oral warts

Note: These guidelines omit detail regarding therapy for anogenital warts.

GUIDELINE CATEGORY

Diagnosis Management Treatment

CLINICAL SPECIALTY

Dermatology

INTENDED USERS

Physicians

GUI DELI NE OBJECTI VE(S)

To provide evidence based recommendations for the treatment of patients with cutaneous warts

TARGET POPULATION

All patients with cutaneous warts

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

- 1. Clinical examination
- 2. Histopathological assessment
- 3. Human papillomavirus (HPV) genotyping
- 4. Differential diagnosis

Treatment

- 1. No treatment
- 2. Destructive treatments
 - Salicylic acid
 - Cryotherapy
 - Thermocautery/curettage and cautery
 - Chemical cautery (silver nitrate stick)
 - Carbon dioxide laser
 - Pulsed dye laser
 - Photodynamic therapy
- 3. Virucidal methods
 - Formaldehyde
 - Glutaraldehyde
- 4. Antimitotic therapy
 - Bleomycin
 - Retinoids
- 5. Immune stimulation
 - Topical sensitization (dinitrochlorobenzene, squaric acid dibutylester, diphencyprone)

Interventions Considered But Not Recommended

Podophyllin/podophyllotoxin, hypnosis, local heat treatment, intralesional interferon, topical imiquimod, irradiation, cimetidine, homeopathy

MAJOR OUTCOMES CONSIDERED

- Side effects of treatment
- Spontaneous regression
- Risk of malignancy
- Lesion response rate
- Lesion recurrence

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- I: Evidence obtained from at least one properly designed, randomized controlled trial
- II-I: Evidence obtained from well designed controlled trials without randomization
- II-ii: Evidence obtained from well designed cohort or case-control analytic studies, preferably from more than one centre or research group
- II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
- III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees
- IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length or comprehensiveness of follow-up or conflicts of evidence)

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

- A. There is good evidence to support the use of the procedure.
- B. There is fair evidence to support the use of the procedure.
- C. There is poor evidence to support the use of the procedure.
- D. There is fair evidence to support the rejection of the use of the procedure.
- E. There is good evidence to support the rejection of the use of the procedure.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines are edited by the Therapy Guidelines and Audit Sub-committee (TGA) and subsequently returned to the task force for revision. The approved draft version is published in the quarterly British Association of Dermatologists (BAD) newsletter, and all BAD members are given the opportunity to respond, positively or negatively, but hopefully helpfully, within three months of publication. Finalised guidelines are approved by the TGA and the Executive Committee of the BAD and finally published in the British Journal of Dermatology.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (I-IV) and strength of recommendation ratings (A-E) are defined at the end of the "Major Recommendations" field.

Diagnosis

Diagnosis of warts is usually based on clinical examination but can be suggested by the histological appearances of acanthotic epidermis with papillomatosis, hyperkeratosis, and parakeratosis, with elongated rete ridges often curving towards the centre of the wart. Dermal capillary vessels may be prominent and thrombosed. There may be large keratinocytes with eccentric pyknotic nuclei surrounded by a perinuclear halo (koilocytes are characteristic of human papilloma virus [HPV]-associated papillomas). HPV infected cells may have small eosinophilic granules and diffuse clumps of basophilic keratohyaline granules. These are not HPV particles. Flat warts have less acanthosis and hyperkeratosis and do not have parakeratosis or papillomatosis.

HPV typing is limited to a few laboratories but may be useful in some cases of genital warts in children with suspected sexual abuse. Knowledge of the HPV genotype in benign warts does not influence choice of therapy.

Differential Diagnosis

Plantar warts must be distinguished from callosities which are ill-defined areas of waxy, yellowish thickening, which on paring reveal no capillaries. Corns occur on pressure points and are usually smaller and painful with a central plug. Plane warts must be distinguished from lichen planus, which will normally show a violaceous discoloration and Wickham's striae. The lesions of lichen planus are usually pruritic and often accompanied by characteristic mucosal lesions. Epidermal naevi may resemble clusters of filiform and digitate warts. The individual lesions of molluscum contagiosum are white umbilicated papules sometimes showing a central depression.

Treatment

There is no single treatment that is 100% effective and different types of treatment may be combined. Research into efficacy of treatment must take into account the possibility of spontaneous regression. It is a valid management option to leave warts untreated if this is acceptable to patients but plantar warts can be painful and hand warts sufficiently unsightly to affect school attendance or cause occupational difficulty. Warts in adults, in those with a long duration of infection, and in immunosuppressed patients are less likely to resolve spontaneously and are more recalcitrant to treatment.

Different types of warts and those at different sites may need differing treatments. Genital warts are not dealt with in depth in these guidelines. Facial warts should not be treated with wart paints because of the risk of severe irritation and possible scarring. Plane warts Koebnerize readily and any destructive technique may exacerbate the problem. The majority of warts can be treated in general practice, and, increasingly, wart clinics are run by nursing staff. A summary of treatments is given in the tables below.

The ideal aims of treatment of warts are: (i) to remove the wart with no recurrence; (ii) to produce no scars; and (iii) to induce life-long immunity. Certain general principles in the treatment of warts should be observed:

- 1. Not all warts need to be treated.
- 2. Indications for treatment are pain; interference with function; cosmetic embarrassment; and risk of malignancy.
- 3. No treatment has a very high success rate (average 60 to 70% clearance in 3 months).
- 4. An immune response is usually essential for clearance. Immunocompromised individuals may never show wart clearance.
- 5. Highest clearance rates for various treatments are usually in younger individuals who have a short duration of infection.

Summary of Treatments for Warts

Strength of Recommendation Quality of Evidence	Treatment	
A, I	Cryotherapy	
B, I	Photodynamic therapy	
B, II-ii	Salicylic acid (SA) Bleomycin Retinoids	
C, II-ii	Formaldehyde	
C, III	Thermocautery Glutaraldehyde	
C, IV	Chemical cautery CO ₂ laser Pulsed dye laser Topical sensitization	
D, I	Cimetidine, oral Homeopathy	
Insufficient Evidence	Podophyllin Folk remedies Hypnosis Heat treatment Interferon Imiquimod	

Treatments for Consideration According to Site of Warts

Face	Hands	Feet	Body
Consider no	Consider no	Consider no	Consider no
treatment	treatment	treatment	treatment
Plane warts	(1)	(1)	Single
Salicylic acid (cream) Cryotherapy Curettage + light cautery	Salicylic acid paint Glutaraldehyde Formaldehyde	Salicylic acid paint Glutaraldehyde Formaldehyde	Curettage + cautery Cryotherapy
Filiform warts	(2)	(2)	Multiple
Cryotherapy Curettage + light	Cryotherapy Curettage + cautery	Cryotherapy Silver nitrate	Cryotherapy Curettage +

Face	Hands	Feet	Body
Consider no	Consider no	Consider no	Consider no
treatment	treatment	treatment	treatment
cautery	Silver nitrate		cautery
	(3)	(3)	Retinoid, systemic
	Photodynamic	 Photodynamic	
	therapy	therapy	
	Bleomycin	Bleomycin	
	CO ₂ laser	CO ₂ laser	
	Pulsed dye laser	Pulsed dye laser	
	Retinoid, systemic	Retinoid, systemic	
	Topical	Topical	
	immunotherapy	immunotherapy	

Notes on table: Published evidence is inadequate to permit development of clear rules for treating particular types of warts in specific sites in individuals of various ages. The above-mentioned therapies could all be considered alone, sequentially, or in combination. Treatment in groups (1) or (2) could be performed by general practitioner but those in group (3) are more specialized.

Destructive Treatments

Salicylic Acid (B, II-ii)

Before application of wart paints, excess keratin should be pared away or filed with sandpaper or emery board and the area softened by soaking in warm water. Collodion-based products form a film that should be peeled off before reapplication. Occlusion has been shown to improve clearance rates of plantar warts.

Cryotherapy (A, I)

Liquid nitrogen (LN_2 , -196 degrees C) is the most commonly used agent. Carbon dioxide slush (-79 degrees C) is now less commonly used. Dimethyl ether/propane mixtures (-57 degrees C) are used because of their convenience but efficacy in inducing tissue temperatures adequate for cell necrosis appears low.

Techniques differ between practitioners with variations in freeze times, mode of application, and intervals between treatment. Many practitioners use a spray, but cotton wool-tipped sticks are still widely used and can be preferable when treating children or for warts near the eyes. It is common practice to freeze until a halo of frozen tissue appears around the wart and then time for 5 to 30 seconds, depending on site and size of wart. When reapplying LN₂ with a cotton stick, it is important to be aware that HPV and other viruses such as human immunodeficiency virus (HIV) can survive in stored liquid nitrogen.

Patients should be warned that cryotherapy is painful and blistering may occur. Caution must be used when freezing warts over tendons and in patients with poor circulation.

Thermocautery/Curettage and Cautery (C, III)

Surgical removal of warts is widely practised, particularly by curettage or blunt dissection, followed by cautery. It may be particularly useful for filiform warts on the face and limbs.

Chemical Cautery: Silver Nitrate Stick (C, IV)

Chemical cautery with repeated daily use of silver nitrate stick can induce adequate destruction to effect wart clearance, but occasionally pigmented scars may develop.

Carbon Dioxide Laser (C, IV)

The destruction produced by the CO_2 laser has been used to treat viral warts. Periungual and subungual lesions, which can be difficult to eradicate by other methods, may be particularly appropriate for this treatment.

Pulsed Dye Laser (C, IV)

The use of the pulsed dye laser depends upon the energy absorption within the capillary loops of the wart and hence localized tissue necrosis. Pain and scarring are less than with the CO_2 laser.

Photodynamic Therapy (B, I)

This treatment depends upon the uptake by abnormal cells of a chemical, usually amino-laevulinic acid (ALA), involved in the porphyrin pathway and subsequent photo-oxidation invoked by irradiation using laser or non-laser light of affected tissue.

Virucidal Methods

Formaldehyde (C, II-ii)

Formaldehyde is virucidal and is available commercially as a 0.7% gel or a 3% solution. As a soak it may hasten clearance of viral warts when combined with regular paring.

Glutaraldehyde (C, III)

Glutaraldehyde is available as a 10% solution or gel and, like formaldehyde, it hardens the skin and makes paring easier

Antimitotic Therapy

Podophyllin/Podophyllotoxin

Podophyllotoxin, the active ingredient within the cruder mixture of podophyllin, acts as an antimitotic by binding to the spindle during mitosis. Cellular division is blocked. The agent is used extensively in the treatment of anogenital warts, but penetration of a thick stratum corneum is poor and podophyllin is much less

effective in the treatment of skin warts. Applied under occlusion after paring of the wart (see Keratolytics section), the treatment may be effective but there is risk of intense inflammation, sterile pustule formation, and secondary infection.

Bleomycin (B, II-ii)

Intralesional application of the cytotoxic agent bleomycin has been used to treat warts that have failed to respond to other modalities of treatment.

Retinoids (B, II-ii)

Retinoids disrupt epidermal growth and differentiation, thereby reducing the bulk of the wart.

Immune Stimulation

Topical Sensitization (C, IV)

The induction of delayed hypersensitivity has been used as a treatment of warts. Dinitrochlorobenzene and squaric acid dibutylester have been used but most studies have looked at the effect of diphencyprone.

Drawbacks of this treatment are that some patients cannot be sensitized whilst others get troublesome eczematous reactions.

Cimetidine (D, I)

Cimetidine has weak, undefined immunomodulatory effects and its use to treat warts has been advocated. Several open trials suggested efficacy, but a controlled trial showed no advantage over placebo.

Other Treatments

Many other treatments have been used to treat warts, although few have received adequate assessment. See the original guideline document for discussion of these treatments

Definitions:

Levels of Evidence

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Recommendation Grades

- A. There is good evidence to support the use of the procedure.
- B. There is fair evidence to support the use of the procedure.
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- D. There is fair evidence to support the rejection of the use of the procedure.
- E. There is good evidence to support the rejection of the use of the procedure.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Consistent and high level of treatment for patients with cutaneous warts

POTENTIAL HARMS

Side Effects of Interventions/Therapies

- Patients should be warned that cryotherapy is painful and blistering may occur. Caution must be used when freezing warts over tendons and in patients with poor circulation. Hypo- and hyper-pigmentation can occur, particularly in black skin. Onychodystrophy can follow treatment of periungual warts.
- Scarring is usual after thermocautery/curettage and cautery.
- Pigmented scars may occasionally develop after chemical cautery with silver nitrate stick.
- Postoperative pain and scarring may occur with use of the carbon dioxide and pulsed dye lasers.

- Glutaraldehyde may stain the skin brown and may cause cutaneous necrosis.
- Pain both on application and afterwards is the main limiting factor for use of bleomycin. The resultant necrosis can cause scarring, pigmentary change, and nail damage. Injected or topical local anaesthesia is often needed.
- Topical sensitization therapy can lead to eczematous reactions in some patients.

CONTRAINDICATIONS

CONTRAINDICATIONS

- The development of scarring is a relative contraindication to thermocautery/curettage and cautery on the sole.
- Bleomycin should not be used in pregnant women since significant absorption of bleomycin has been reported following intralesional injection.

QUALIFYING STATEMENTS

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- These guidelines, prepared on behalf of the British Association of Dermatologists, the British Association of Plastic Surgeons and in consultation with members of the Faculty of Clinical Oncology of the Royal College of Radiologists, reflect the best published data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not be necessarily deemed negligent
- It is important that these guidelines are used appropriately in that they can
 only assist the practitioner and cannot be used to mandate, authorise, or
 outlaw treatment options. Of course it is the responsibility of the practising
 clinician to interpret the application of guidelines, taking into account local
 circumstances.
- Guidelines are inherently a fluid, dynamic process and will be updated on the British Association of Dermatologists (BAD) Web site on a regular basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Potential Audit Points

- 1. Liquid nitrogen cryotherapy: is the treatment regimen used in accordance with recommended frequency, duration, etc., and what is the clearance rate?
- 2. Topical salicylic acid: is the treatment used in a regimen most likely to produce an effect and what is the clearance rate?

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about <u>availability</u>, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Sterling JC, Handfield-Jones S, Hudson PM. Guidelines for the management of cutaneous warts. Br J Dermatol 2001 Jan; 144(1): 4-11. [51 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan

GUIDELINE DEVELOPER(S)

British Association of Dermatologists

SOURCE(S) OF FUNDING

British Association of Dermatologists

GUIDELINE COMMITTEE

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: J.C. Sterling, Department of Dermatology, Addenbrooke's Hospital. Cambridge, UK; S. Handfield-Jones, West Suffolk Hospital, Bury St Edmunds, UK; P.M. Hudson, Peterborough District Hospital, Peterborough, UK

Committee Members: N.H. Cox (Chairman); A. Anstey, C. Bunker; M. Goodfield; A. Highet; D. Mehta; R. Meyrick Thomas; J. Schofield

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

None stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the <u>British Association of Dermatologists Web site</u>.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

• Griffiths CE. The British Association of Dermatologists guidelines for the management of skin disease Br J Dermatol. 1999 Sep; 141(3): 396-7.

Electronic copies: Available in Portable Document Format (PDF) from the <u>British Association of Dermatologists Web site</u>.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 25, 2005. The information was verified by the guideline developer on August 16, 2005.

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